Abstract

Prostate cancer is one of the most abundant types of cancer among men and the demand for a specific treatment is very high. In this thesis, I have focused on using Glutamate Carboxypeptidase II (GCPII), as a target for a proof-of-principle delivery system. GCPII is a transmembrane protein that internalizes after a binding of a ligand and is overexpressed in prostate cancer.

Virus-like particles from Murine polyomavirus (VLPs) are a suitable nanocarrier for the delivery of imaging agents and drugs. Here I describe modifying these VLPs with inhibitors of GCPII and fluorescent dyes and characterize their binding to GCPII on surface plasmon resonance and to cells expressing GCPII on confocal microscopy.

VLPs carrying a GCPII inhibitor show specific binding to GCPII on surface plasmon resonance, however they bind non-specifically to cells that don't express GCPII. Several approaches have been tried to avoid that. The substitution of BC loop on the exterior surface of VLPs that is partially responsible for the binding of sialic acid did not seem to affect specificity on cells. Another approach tested was coating of the wild-type VLPs with large polymer carrying a fluorescent label and a GCPII inhibitor. After the conjugation of the polymer to the VLP, specific binding and internalization in GCPII-positive cells has been achieved in preliminary experiments. Further analysis will be necessary to confirm this finding.

Keywords: Virus-like particles, Glutamate carboxypeptidase II, GCPII, PSMA, targeted delivery, Murine polyomavirus, prostate adenocarcinoma